REMARKS

Claims 1-37, 77, 83-95, 97-108 and 118-123 are now pending in the application. Claims 96 and 124-126 are currently cancelled. Claims 83-95, 98-108 and 118-123 are currently under examination. Amendments have been made to claims 83, 88-92, 95, 98-100, 118, 121, and 122. The Examiner is respectfully requested to reconsider and withdraw the rejection(s) in view of the amendments and remarks contained herein.

OBJECTIONS AND REJECTIONS WITHDRAWN

Applicants acknowledge and thank the Examiner for the withdrawal of the objections and rejections to the specification and claims as detailed in the present Office Action at pages 3-6.

REJECTIONS MAINTAINED

REJECTION UNDER 35 U.S.C. § 112, 1ST PARAGRAPH

Claims 118, 121, 122 and 124-126 stand rejected under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained for reasons of record as set for the in the Office Action of 11/7/06 and 7/19/07. This rejection is respectfully traversed.

Applicants maintain that Claims 118, 121, 122 and 124-126 are fully enabled as required by 35 U.S.C. § 112, par. 1 and as further explained in MPEP § 2107.03, section III. Applicants appreciate the detailed reasoning and reference provided by the Examiner. However, the Applicants respectfully disagree with the conclusion that one of ordinary skill in the art could not reasonably make the correlation or prediction that from a single animal model using a single clonotypic tumor with a single Vaccibody that

any Vaccibody embodiment could be used in vivo to treat or prevent any disease much less multiple myeloma in any animal including human. (Action at page 10). Applicants respectfully submit that the reference provided in support of a finding of non-enablement is inapposite to the present case for enablement. Voskoglou-Nomikos et. al. fails to compare immunogenic/vaccine based cancer drugs and their rates of preclinical success. Further, the cited reference fails to compare myeloma and lymphoma tumors with any cancer treatments. Applicants note that the cited reference states: "The use of preclinical cancer models for selection of potential cancer therapeutics was pioneered by the NCI in the United States in the mid-1950s. The screening strategies used until 1990 were essentially compound oriented and involved a small number of predominantly murine allograft tumors, with emphasis on leukemia (1–7). Several studies from the NCI and others demonstrated that this approach had low clinical predictive value for activity in Phase II trials (5–9) and yielded compounds with selective activity toward human leukemias and lymphomas (10 –12). (Voskoglou-Nomikos et. al. page 4227, col. 2, last par. to page 4228, col. 1, 1st par). Hence, the use of mouse allografts in preclinical cancer screening was successful in identifying human lymphoma selective cancer drugs. Applicants further note, that the present anti-tumor agents are vaccibodies that require a functional immune system. The suggestion that human xenograft tumor models are superior in this particular case are contrary to the method of operation of the present therapeutic approach. In order to utilize a human xenograft tumor model in the present technology, an immunodeficient mouse model would be required, since a functioning immune system in the host would obviously react with the human xenograft and no or little information could be gathered as to the efficacy of the

therapeutic agent. Since the present technology requires a functioning immune system for the generation of the vaccibodies of the present invention, an immunodeficient mouse model would not work to generate the needed B-cell and T-cell immunological responses. In conclusion, the present technology incorporating vaccibodies, i.e. an immunological therapeutic agent against multiple myeloma and lymphoma which has a mechanism of action that is distinct to the chemotherapeutic agents discussed in the cited reference, and as such, the conclusions based in that reference are applicable to chemotherapeutic agents and not immunological based therapeutic agents.

Although no admission is made herein by the Applicants that Claims 118, 121, 122 and 124-126 are not fully enabled, in the interest of advancing prosecution, the Applicants have amended Claims 121 and 122 and have cancelled Claims 124-126 without prejudice or disclaimer. Claims 121 and 122 now refer to a "composition" comprising the nucleic acid fragment of Claim 83 or the vector of Claim 119 in admixture with a carrier. Applicants believe any issues under 35 U.S.C. §112, 1st par. concerning the intended use as a vaccine/pharmaceutical form of the composition should therefore be moot.

With respect to Claim 118, Applicants note that the claim language merely requires that the isolated nucleic acid fragment of Claim 83 be formulated "to be administered to a patient to induce production of said antibody based dimeric molecule". Further, Claim 83 requires that the injection of the isolated nucleic acid molecule in a "patient" leads to production in the patient of the expression product of the isolated nucleic acid molecule. Hence, Claim 83 does not require that the patient raise an immune response against the expression product. In light of the existing knowledge in

the art pertaining to nucleic acid vaccination, which has amply demonstrated that expression of an injected nucleic acid molecule can be easily accomplished, the subject matter of Claim 118 is indeed enabled by the specification. In this context, an animal (in this case murine) model is more than sufficient to prove that the constructs of Claim 83 can be expressed in a mammal when administered as taught in the specification.

NEW GROUNDS FOR OBJECTION

CLAIM OBJECTIONS

Claim 83 is objected to for a grammatical error. Applicants have amended Claim 83 to overcome this objection.

Claims 96 and 98 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicants respectfully submit that the cancellation of Claim 96 has obviated the present objection.

Accordingly, Applicants respectfully request that the objections be reconsidered and withdrawn.

NEW GROUNDS FOR REJECTION

REJECTION UNDER 35 U.S.C. § 101

Claims 83, 88-92, 95, 96, 98-100 and 118-126 are rejected under 35 U.S.C. §101 as being directed to a nucleic acid. The Examiner contends that the claims read on a nucleic acid that is found in nature and therefore do not constitute patentable subject matter.

Applicants have amended Claim 83 to recite: "An isolated nucleic acid encoding a monomer unit of a recombinant antibody-based dimeric molecule..." as recommended by the Examiner. Therefore, all claims directly and indirectly dependent on Claim 83, which include Claims 88-92, 95, 96, 98-100 and 118-126 incorporate an isolated nucleic acid in compliance with 35 U.S.C. §101. Applicants respectfully request the Examiner reconsider and withdraw the rejection of Claims 83, 88-92, 95, 96, 98-100 and 118-126 under 35 U.S.C. §101.

REJECTION UNDER 35 U.S.C. § 112, 2ND PARAGRAPH

Claims 83, 88-92, 95, 96, 98-100 and 109-126 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which Applicant regards as the invention. This rejection is respectfully traversed.

Applicants respectfully submit that the present amendment to Claims 83, 100 and 118 as well as for the reasons stated above with respect to the §112, 1st paragraph rejections, overcome the present under 35 U.S.C. § 112, second paragraph.

With respect to Claim 83, the isolated nucleic acid encodes a monomer unit wherein each of said monomer unit comprises a targeting unit for an antigen presenting cell and an antigenic unit for an antigen presenting cell, and wherein said monomer unit each lack a CH2 domain. The antigen presenting cell requires both the targeting unit for binding and the antigenic unit for antigen processing to express surface idiotypic determinant molecules on the antigen presenting cell encoded by the antigenic unit. (See Specification at page 14 – page 16 and Figures 1 and 2).

With respect to Claim 100, Applicants have amended Claim 100 to recite: "The isolated nucleic acid of claim 99, wherein said antigenic scFv has VL and VH chains from a monoclonal Ig produced by myeloma or lymphoma." The changes made to Claim 100 clarifies that the antigenic scFv are derived from a monoclonal Ig comprising the VL and VH domains of the monoclonal Ig. Applicants respectfully submit that any indefiniteness is removed by the present amendment to Claim 100.

With respect to Claim 118, Applicants believe that the amendment to Claim 118 renders the metes and bounds of the claim clear. Claim 118 has been amended to recite: "The isolated nucleic acid of claim 83, formulated for administration to a patient to induce production of said recombinant antibody-based dimeric molecule." Claim 83 recites "recombinant antibody-based dimeric molecule". Therefore any antecedent basis errors have been rendered moot.

The Action further alleges that Claim 118 is indefinite because it is not clear whether formulated nucleic acid of Claim 118 would express the monomer encoded by the nucleic acid or is formulated to express two monomer units in order to produce the recombinant antibody based dimeric molecule. As discussed on page 5 and 6 with respect to the withdrawal of the rejection of Claim 118 under 35 U.S.C. §112, 1st paragraph, dimmers are formed from homodimers, which can assemble spontaneously. In other words, the assembly of the monomeric units into the dimeric molecule antibody-like molecule is spontaneous in the cell and can be produced by having one single copy of a nucleic acid of the invention expressed in a cell, there is, however, nothing which precludes e.g. a muscle cell from taking up two or more of the claimed molecules and express these, and as a consequence, the dimeric expression product can either be

derived from one single or 2 nucleic acids of the invention. However, the resulting expression products (the dimeric molecules) are identical irrespective of whether they are derived from expression of 1 or 2 nucleic acids.

Applicants respectfully request that the present rejection of Claim 118 under 35 U.S.C. §112, 2nd paragraph be reconsidered and withdrawn accordingly.

CONCLUSION

It is believed that a full and complete response has been made to all of the issues raised in the outstanding Office Action and Advisory Action. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

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